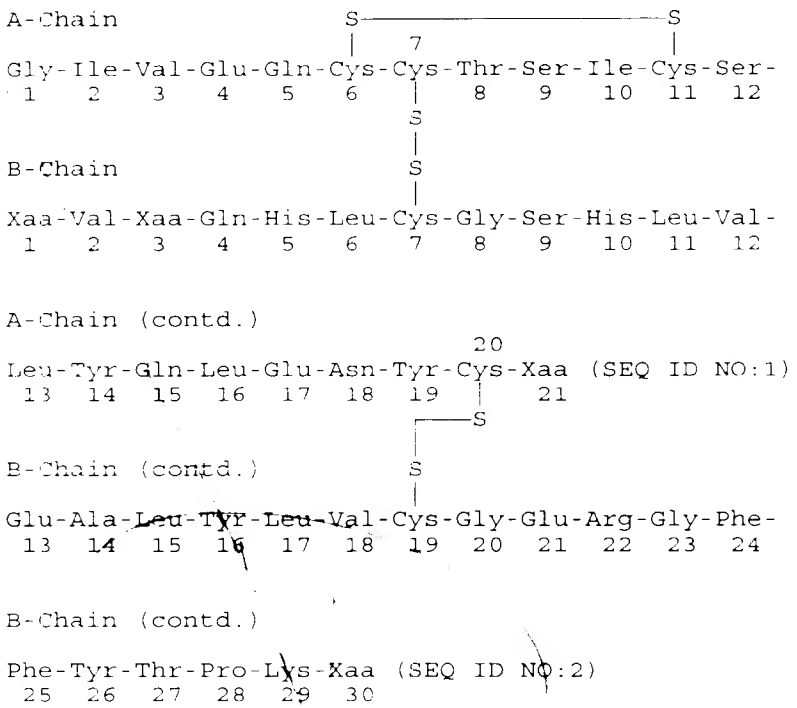
68. An insulin derivative having the following sequence:



wherein

(a) Xaa at positions A21 and B3 are, independently, any amino acid residue which can be coded for by the genetic code except Lys, Arg and Cys;

(b) Xaa at position B1 is Phe or is deleted;

(c) Xaa at position B30 is any amino acid residue which can be coded for by the genetic code except Lys, Arg and Cys; and

(d) the ε-amino group of Lys^{B29} is substituted with a lipophilic substituent having at least 6 carbon atoms;

wherein the insulin derivative is a Zn^{2+} complex and the Zn^{2+} complex of the insulin derivative is more water soluble than the insulin derivative without Zn^{2+}.

69. The insulin derivative of claim 68, wherein Xaa at position A21 is Asn

71. The insulin derivative of claim 68, wherein Xaa at position B1 is deleted.

72. The insulin derivative of claim 68, wherein Xaa at position B1 is Phe.

73. The insulin derivative of claim 68, wherein Xaa at position B3 is Asn, Asp, Gln or Thr.

74. The insulin derivative of claim 68, wherein Xaa at position B30 is Ala or Thr.

75. The insulin derivative of claim 68, wherein Xaa at position A21 is Ala, Asn, Gln, Gly or Ser, Xaa at position B3 is Asn, Asp, Gln or Thr, and Xaa at position B30 is Ala or Thr.

76. The insulin derivative of claim 68, wherein Xaa at position A21 is Asn, Xaa at position B3 is Asn, Xaa at position B1 is Phe and Xaa at position B30 is Thr.

77. The insulin derivative of claim 68 which is in the form of a hexamer.

78. The insulin derivative of claim 77, wherein Xaa at position A21 is Asn, Xaa at position B1 is Phe, Xaa at position B3 is Asn, and Xaa at position B30 is Thr.

79. The insulin derivative of claim 77, wherein two zinc ions bind to the hexamer.

80. The insulin derivative of claim 77, wherein three zinc ions bind to the hexamer.

81. The insulin derivative of claim 77, wherein four zinc ions bind to the hexamer.

82. A pharmaceutical composition which is an aqueous solution, comprising (a) an insulin derivative of claim 68, (b) an isotonic agent, (c) a preservative and (d) a buffer.

84. The pharmaceutical composition of claim 82, wherein the solubility of the insulin derivative exceeds 600 nmol/ml of the aqueous solution.

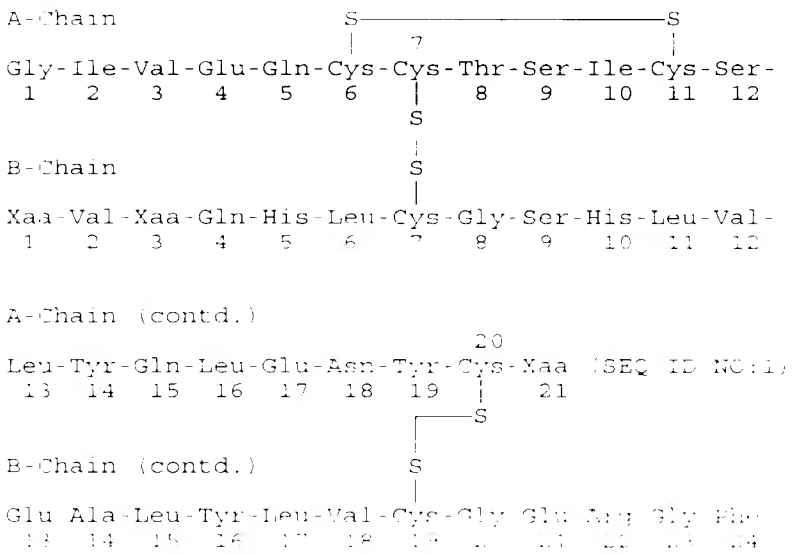
85. The pharmaceutical composition of claim 82, further comprising an insulin or an insulin analogue which has a rapid onset of action.

86. The pharmaceutical composition of claim 82, wherein Xaa at position A21 is Asn, Xaa at position B3 is Asn, Xaa at position B1 is Phe and Xaa at position B30 is Thr.

87. The pharmaceutical composition of claim 82, wherein the insulin derivative is in the form of a hexamer.

88. A method of treating diabetes in a patient in need of such a treatment, comprising administering to the patient a therapeutically effective amount of a pharmaceutical composition of claim 82.

89. An insulin derivative having the following sequence:



wherein

(a) Xaa at positions A21 and B3 are, independently, any amino acid residue which can be coded for by the genetic code except Lys, Arg and Cys;

(b) Xaa at position B1 is Phe or is deleted;

(c) Xaa at position B30 is deleted; and

(d) the ϵ-amino group of Lys^{B29} is substituted with a lipophilic substituent having at least 6 carbon atoms.

90. The insulin derivative of claim 89, wherein Xaa at position A21 is Ala, Asn, Gln, Gly or Ser.

91. The insulin derivative of claim 90, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

92. The insulin derivative of claim 89, wherein Xaa at position B1 is deleted.

93. The insulin derivative of claim 92, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

94. The insulin derivative of claim 89, wherein Xaa at position B1 is Phe.

95. The insulin derivative of claim 94, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

96. The insulin derivative of claim 89, wherein Xaa at position B3 is Asn, Asp, Gln or Thr.

97. The insulin derivative of claim 96, wherein the lipophilic substituent has from 12 to 24 carbon atoms

98. The insulin derivative of claim 89, wherein Xaa at position B3 is Asn, Asp, Gln or Thr

99. The insulin derivative of claim 98, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

100. The insulin derivative of claim 89, wherein Xaa at position A21 is Asn, Xaa at position B1 is Phe, and Xaa at position B3 is Asn.

101. The insulin derivative of claim 100, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

102. The insulin derivative of claim 89, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

103. The insulin derivative of claim 89, wherein the lipophilic substituent is cyclohexylvaleroyl.

104. The insulin derivative of claim 89, wherein the lipophilic substituent is acyl-glutamyl wherein the acyl is a linear, saturated acyl having 6 to 24 carbon atoms.

105. The insulin derivative of claim 89, wherein the lipophilic substituent is lauroyl.

106. The insulin derivative of claim 89, wherein the lipophilic substituent is myristoyl.

107. The insulin derivative of claim 89, wherein the lipophilic substituent is palmitoyl.

108. The insulin derivative of claim 89, wherein the lipophilic substituent is 2-succinylamido myristic acid.

109. The insulin derivative of claim 89, wherein the lipophilic substituent is 2-succinylamido palmitic acid.

2-succinylamidoethyloxy palmitic acid

111. The insulin derivative of claim 89, wherein the lipophilic substituent is myristoyl-α-glutamyl.

112. The insulin derivative of claim 89, wherein the lipophilic substituent is myristoyl-α-glutamyl-glycyl.

113. The insulin derivative of claim 89, wherein the lipophilic substituent is choloyl.

114. The insulin derivative of claim 89, wherein the lipophilic substituent is 7-deoxycholoyl.

115. The insulin derivative of claim 89, wherein the lipophilic substituent is lithocholoyl.

116. The insulin derivative of claim 89, wherein the lipophilic substituent is lithocholoyl-glutamyl.

117. The insulin derivative of claim 89, wherein the lipophilic substituent is 4-benzoyl-phenylalanine.

118. The insulin derivative of claim 89, wherein the lipophilic substituent is L-thyroxyl.

119. The insulin derivative of claim 89, wherein the lipophilic substituent is suberoyl-D-thyroxine.

120. The insulin derivative of claim 89, wherein the lipophilic substituent is 3,3',5,5'-tetraiodothyroacetyl.

121. The insulin derivative of claim 89, wherein the lipophilic substituent is an acyl group having at least 10 carbon atoms.

Hexadecanoyl

123. The insulin derivative of claim 89 which is in the form of a hexamer.

124. The insulin derivative of claim 123, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

125. The insulin derivative of claim 123, wherein Xaa at position A21 is Asn, Xaa at position B3 is Asn, and Xaa at position B1 is Phe.

126. The insulin derivative of claim 123, wherein two zinc ions bind to the hexamer.

127. The insulin derivative of claim 126, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

128. The insulin derivative of claim 123, wherein three zinc ions bind to the hexamer.

129. The insulin derivative of claim 128, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

130. The insulin derivative of claim 123, wherein four zinc ions bind to the hexamer.

131. The insulin derivative of claim 130, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

132. A pharmaceutical composition which is an aqueous solution, comprising (a) an insulin derivative of claim 89, (b) an isotonic agent, (c) a preservative and (d) a buffer.

133. The pharmaceutical composition of claim 132, wherein the pH of the aqueous solution is in the range of 6.5-8.5.

135. The pharmaceutical composition of claim 132, further comprising an insulin or an insulin analogue which has a rapid onset of action.

136. The pharmaceutical composition of claim 132, wherein Xaa at position A21 is Asn, Xaa at position B3 is Asn, and Xaa at position B1 is Phe.

137. The pharmaceutical composition of claim 132, wherein the lipophilic substituent has from 12 to 24 carbon atoms.

138. The pharmaceutical composition of claim 132, wherein the insulin derivative is in the form of a hexamer.

139. A method of treating diabetes in a patient in need of such a treatment, comprising administering to the patient a therapeutically effective amount of a pharmaceutical composition of claim 132.

140. An insulin derivative having the following sequence: